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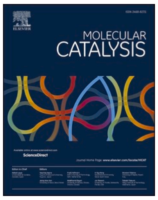

Cu_2O/TiO_2 as a sustainable and recyclable photocatalyst for gram-scale synthesis of phenols in water

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ABSTRACT

A green and straightforward protocol was developed for the synthesis of phenols from aryl boronic acid using an inexpensive and available Cu_2O/TiO_2 photocatalyst under visible light and sunlight. This approach proceeded in mild reaction conditions in water and the presence of air as a green oxidant, resulting in the corresponding phenols in good to excellent yields. Sunlight was also a sustainable source for this photochemical reaction. Heterogeneous nano photocatalyst was successfully recovered in 8 consecutive runs. It is noteworthy that, the photocatalyst exhibited high activity for the large-scale synthesis of phenols.

Introduction

The last decade has witnessed remarkable progress of photoredox catalysts particularly in the organic chemistry field.[1] Indeed in many cases, these catalysts could effectively proceed with the conventional or non-proceeded organic transformations in milder and safer pathways which well meet the principles of green chemistry. In this line, semiconductors as cost-effective and benign photocatalysts have attracted a lot of attention. But most common and popular semiconductors such as TiO_2 could not be applied for all photocatalytic targets in the visible-light region due to its wide bandgap and rapid recombination of photogenerated electron/hole (e^-/h^+) pairs. Thus, many efforts have been devoted to the development of procedures based on an effective visible-light-driven-photocatalyst. One of these promising approaches is hetero-junctions with other materials, particularly, p-type Cu_2O semiconductor due to the environmentally friendly, non-toxicity, and cost-effectiveness of It. [2]' [3]

Phenols and their derivatives are privileged compounds often used in the synthesis of valuable natural and pharmaceutical products.[4] Among the various procedures to the synthesis of phenols the oxidative hydroxylation of boronic acids is more considerable due to the easy availability and low toxicity of phenylboronic acid derivatives. To this end various catalytic systems have been introduced including AgNP montK-10,[5] Ru@imine-nanoSiO_2,[6] Pd/bentonite,[7] acidic Al_2O_3,[8] GO,[9] Au-PVP,[10] *etc.*[11] Although these catalysts demonstrated high reactivity toward this transformation, they suffer from some drawbacks such as using strong oxidants, bases, and non-environmentally solvents. Besides these catalysts, photocatalysts have been also employed to change harsh reaction conditions to milder (Scheme 1).[11-17]

Recently, we synthesized and characterized Cu_2O/TiO_2 and successfully employed it as a photocatalyst for the synthesis of aryl phosphonates under visible light.[18] In this study by using this privileged photocatalyst, we prepared various phenols *via* visible-light mediated oxidative hydroxylation in water as a green solvent and gram- scale.

Experimental

General information

Phenylboronic acid derivatives were commercially available. All other reagents and all solvents were obtained from commercial sources and purified using standard methods. Column chromatography was accomplished on small columns of silica gel. ^1H NMR (300 MHz) and ^{13}C NMR (76 MHz) spectra were run on Bruker Avance DRX in pure deuterated chloroform (CDCl3). Chemical shifts are given in the δ scale in part per million (ppm) and J in Hz. Data for 1H NMR are reported as follows: chemical shift (δ ppm), multiplicity (s= singlet, d= doublet, t= triplet, q= quartet, m= multiplet, dd= doublet of doublets, ddd= doublet of doublet of doublet, td= triplet of doublet), coupling constants (Hz), and integration. Melting points were determined in open capillary tubes in a Buchi-510 oil melting point apparatus. Power X-ray diffraction patterns were recorded with Cu Kα (λ= 1.54178 Å) radiation. Scanning electron microscopy (SEM) was done at TESCAN-Vega 3. The

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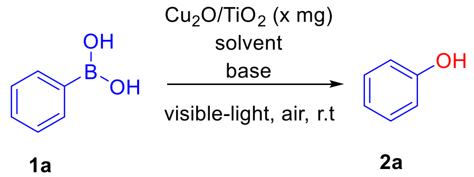
Table 1
The effect of various reaction conditions on the hydroxylation of phenylboronic acid.[a]



Entry	PC (x mg)	Solvent	Base	Light	Time (h)	Yield (%)
1	5	H_2O	K_2CO_3	White	4	90
2	5	CH_3CN	K_2CO_3	White	4	35
3	5	EtOH	K_2CO_3	White	4	40
4	5	Toluene	K_2CO_3	White	4	trace
5	5	DMSO	K_2CO_3	White	4	20
6	5	CH_3CN/H_2O (1:9)	K_2CO_3	White	4	65
7	5	H_2O	K_2CO_3	White	2	40
8	5	H_2O	K_3PO_4	White	4	70
9	5	H_2O	Na_2CO_3	White	4	40
10	5	H_2O	NaOH	White	4	50
11	5	H_2O	Cs_2CO_3	White	2	91
12	5	H_2O	NEt_3	White	4	75
13	5	H_2O	-	White	4	35
14	5	H_2O	K_2CO_3	Blue	4	70
15	5	H_2O	K_2CO_3	Green	4	50
16	5	H_2O	K_2CO_3	Red	4	20
17	5	H_2O	K_2CO_3	Violet	4	35
18	5	H_2O	K_2CO_3	-	8	10
19	3	H_2O	K_2CO_3	White	4	50
20	10	H_2O	K_2CO_3	White	4	92
21	-	H_2O	K_2CO_3	White	8	trace
22[b]	5	H_2O	K_2CO_3	White	8	8
23	Cu_2O (5)	H_2O	K_2CO_3	White	4	45
24	TiO_2 (5)	H_2O	K_2CO_3	White	4	30

[a] Reaction conditions: phenylboronic acid (0.3 mmol), Base (0.3 mmol), Solvent (0.5 ml), under air, room temperature, isolated Yield.
[b] under argon atmosphere.

amount of nanoparticles (Cu and Ti) was measured by inductively coupled plasma (ICP, Varian, Vista-pro). The lamps for irradiation were compact fluorescent lamps (CFL) 15 W white, blue LED 12 W, green LED 12 W, red LED 12 W and violet LED 40 W.

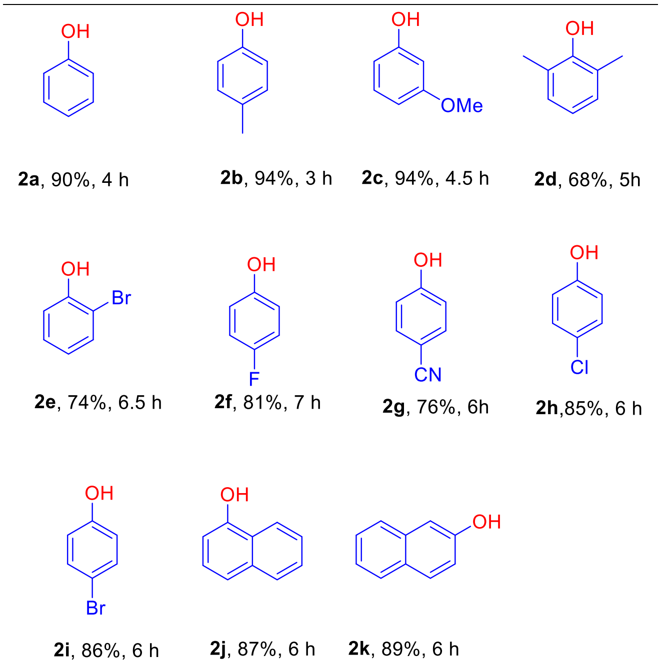
Preparation of Cu_2O/TiO_2 photocatalyst[18]

Cu_2O/TiO_2 nanostructure composite oxides were synthesized via the modified subsequent method. In this way, 13.2 g (0.066 mol) of cupric acetate monohydrate was dissolved in 600 mL of distilled water, and then 3.2 mL (0.011 mol) of PEG-300 was added under vigorous stirring. Subsequently, tetrabutyl titanate (0.002 mmol, 0.7 g dissolved in 3 mL of ethanol) was added dropwise into the resulting suspension of cupric acetate. After producing a white precipitate, NaOH (5mL, 5 M) and hydrazine (15 mL, 5 M) were added dropwise under stirring at room temperature. The resulting mixture was kept at 12–14 °C for 15 min. After that, nanoparticles were collected using a centrifuge and washed with water (500 mL) and acetone (50 mL). Finally, the material was dried in a vacuum oven for 3 h at 90°C. The resulting material contained 6 mol% Ti and 31 mol % Cu.

General procedure for the ipso-hydroxylation of aryl boronic acids using Cu_2O/TiO_2 photocatalyst

Under air atmosphere, Cu_2O/TiO_2 (0.5 mol %, 5 mg) was added to a mixture of aryl boronic acid (0.3 mmol), K_2CO_3 (0.3 mmol, 41.46 mg), and H_2O (0.5 mL) and then stirred at 25 °C under irradiation of white LEDs (15 W) (note that the reaction temperature was maintained by circulating cooling water), the reaction was monitored by TLC. After the reaction was completed and separation of the catalyst by centrifuge, the reaction mixture was extracted with EtOAc and water. The organic layer was dried over anhydrous Na_2SO_4 and the solvent was then removed under reduced pressure to get the crude product. Pure products were obtained after column chromatography on silica using *n*-hexane and ethyl acetate mixture as eluent.

Table 2
Scope of phenylboronic acids.[a,b]



[a] Reaction conditions: aryl boronic acid (0.3 mmol), K_2CO_3 (0.3 mmol), H_2O (0.5 ml), under air atmosphere irradiated with a 15 W LED. [b] Isolated Yield.

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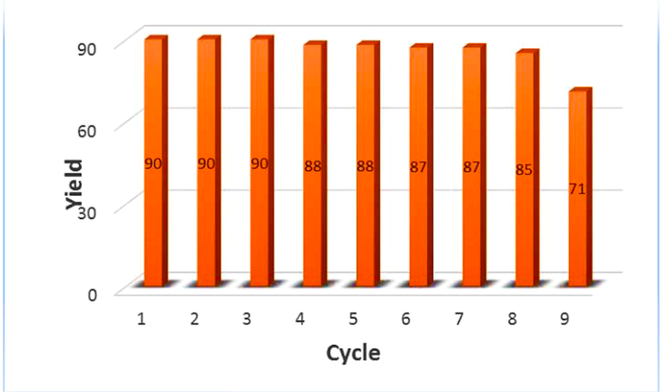


Fig. 1. Recovery of Cu_2O/TiO_2 photocatalyst for the reaction of phenylboronic acid.

Results and discussion

First, our study was devoted to the synthesis of Cu_2O/TiO_2 photocatalyst via our previous report.[18] To evaluate the potential of this photocatalyst for the synthesis of phenols, phenylboronic acid was

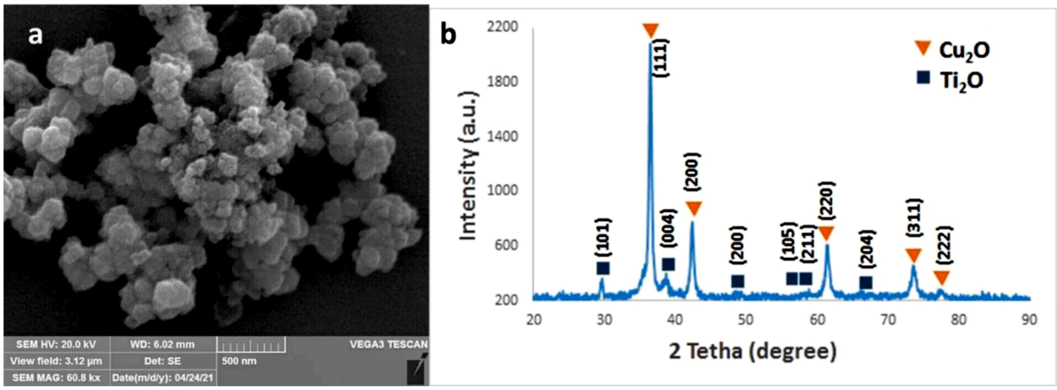
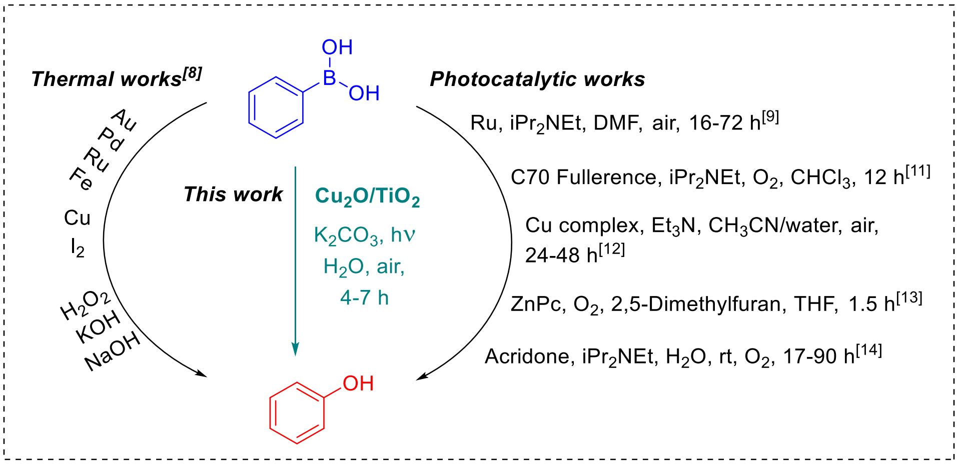
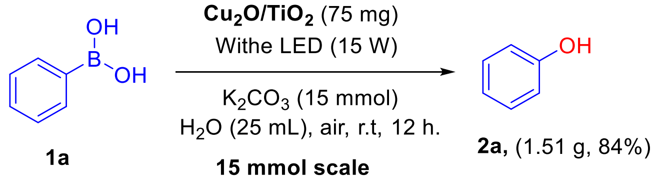


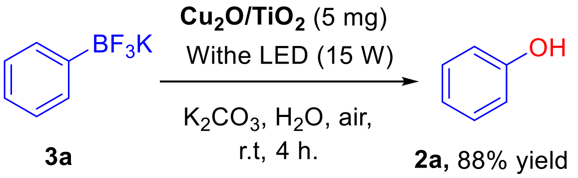
Fig. 2. a) SEM image and b) XRD pattern of the Cu_2O/TiO_2 nanoparticles after eight runs.



Scheme 1. Various conditions for oxidative hydroxylation of boronic acids.



Scheme 2. Gram-scale synthesis of phenol.

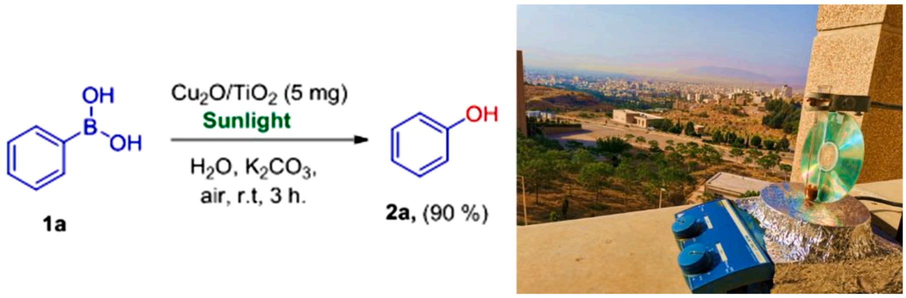


Scheme 3. Synthesis of phenol from potassium phenyl trifluoroborate using Cu_2O/TiO_2 catalyst.

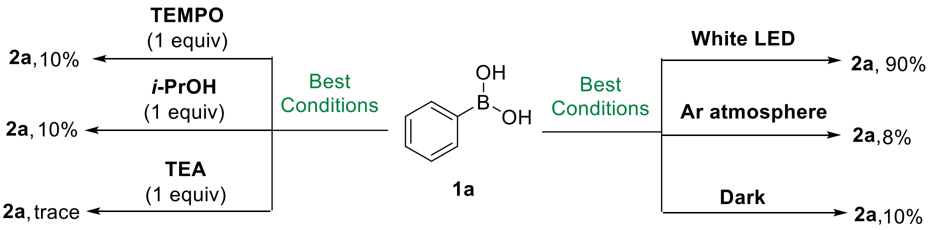
chosen as a model substrate. To start optimizing the reaction condition, first, the effect of solvent was tested in the presence of K_2CO_3 under irradiation with white LED (15 W) using atmospheric air as an oxidant, and water was found to be the best solvent. The model reaction then took place in the presence of different organic and inorganic bases. Although Cs_2CO_3 gave the same result in a shorter reaction time, K_2CO_3 was selected as the best from an economic point of view. As well, in the absence of a base 35% yield was only obtained. In the next step, we change the source of light, and the reaction was carried out in the presence of blue, green, and purple lights, and a higher yield was obtained using white LED. It is also worth mentioning that conducting the reaction in the absence of light under the same reaction conditions led to a much lower yield (10% within 8h), indicating the key role of light (Table 2, entry 18). The reaction conditions were next surveyed by employing the different amounts of catalyst (Table 2, entries 19-21), among them 5 mg was found to afford the best result under the otherwise mentioned reaction condition (entry 1). The yield of the reaction was significantly decreased in the presence of an argon atmosphere, indicating the key role of air as an oxidizing agent. For comparison, the reaction was conducted using Cu_2O and TiO_2 (P25) alone as photocatalyst under obtained optimal reaction conditions (Table 1, entries 23, 24). As expected in these cases the desired product was obtained in a lower yield than Cu_2O/TiO_2 as photocatalyst.

Encouraged by this promising data, we then tested the scope and generality of the present system for various phenylboronic acids (Table 2). Aryl boronic acids with donating substituent at *para* position (**2b**) delivered a higher yield than electron-withdrawing groups in the same position (**2f-i**). Interestingly, this photocatalytic system could successfully be applied for *ortho*-substituted phenylboronic acid which suffers from steric hindrance but in lower yields (**2d, 2e**). Furthermore, 1-naphthalenylboronic acid, and 2-naphthalenylboronic acid also successfully participated in the reaction, furnishing the corresponding products in good yields (**2j, 2k**). It should be noted that in all cases no by-products were not observed.

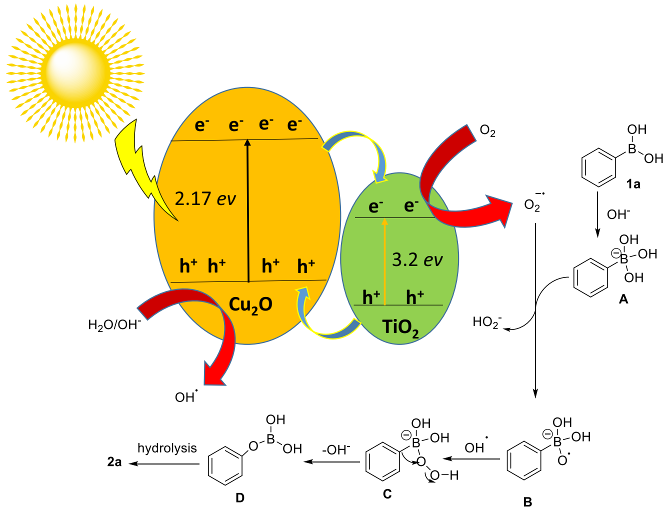
To further demonstrate the high potential and efficiency of this



Scheme 4. Synthesis of phenol under sunlight irradiation.



Scheme 6. Control experiments.



Scheme 7. Proposed mechanism.

system, a scale-up reaction of phenylboronic acid (1.83 g, 15 mmol) was investigated. As shown in Scheme 2, phenol product could be successfully obtained in 84% yield (1.51 g), albeit in a longer reaction time (12 h).

Further studies revealed that the present photocatalytic system could successfully be employed for the synthesis of phenol from potassium phenyl trifluoroborate in 88% yield (Scheme 3).

In the next step, the model reaction was conducted under sunlight as shown in scheme 4. The maximum temperature of the day was 28°C and the minimum was 26°C. Interestingly, under these conditions the phenol product was obtained in 90% within 3 h. an Increase in the reaction rate is due to the higher intensity of sunlight compared to the LEDs.

Due to the importance of reusability of heterogeneous catalysts from industry and economical point of view, in the next part of this study, we checked the reusability of Cu_2O/TiO_2 photocatalyst for the model reaction. Fortunately, our photocatalyst could be reused 8 times without loss of activity, demonstrating the high efficiency of our protocol to the synthesis of phenol derivatives in the green pathway (Fig. 1).

To investigate the structural deviations and stability of the catalyst, the recovered catalyst after 8 runs was analyzed with SEM, XRD, and ICP. The SEM image of the recovered catalyst (Fig. 2a) showed that the Cu_2O/TiO_2 photocatalyst could successfully maintain its structure during the recovery process. Furthermore, the XRD spectra of the recovered catalyst well established no obvious structural changes (Fig. 2b). Based on the ICP analysis the recovered catalyst contained 6 mol% Ti and 31 mol% Cu like the fresh catalyst. Together, these data indicated that the nano photocatalyst is highly stable against aggregation or collapse even after several at the present study.

Finally, we performed some control experiments[19-21] under identical conditions to confirm that the reaction took place through a radical pathway (Scheme 6). When the reaction was conducted in the presence of TEMPO (1 equiv) as a radical scavenger only 10 % yield of the phenol was obtained, as well as the reaction in the presence of triethanolamine (TEA) as hole scavenger could not proceed even after 12 h. Moreover, as described in Table 1, the reaction in the absence of light could not proceed. These observations led us to propose a mechanism based on the radical pathway. As shown in Scheme 7 photoexcitation of TiO_2/Cu_2O nanoparticles generated electrons and holes (e^-/h^+). First, electrons in the TiO_2 side of catalysts converted the O_2 into $O_2^{\bullet -}$, which generated intermediate **B** via a single electron transfer process. This intermediate coupled with hydroxyl radical formed via holes of photocatalyst to deliver intermediate **C**. Subsequently aryl group migration from boron to oxygen followed by losing OH produced boronate ester **D**. consequently the corresponding phenol **2a** was obtained by hydrolysis process.

Conclusion

In this study, we successfully employed Cu_2O/TiO_2 as a sustainable and durable photocatalyst for the synthesis of phenol derivatives via a radical pathway under visible light. Advantages of this protocol are the use of water as a green solvent, and air as green and inexpensive oxidant, broad substrate scope, and high functional group tolerance. This promising protocol not only delivered phenol derivatives in good to excellent yield but could also be applied for their gram-scale synthesis. Remarkably, this heterogeneous photocatalyst could be reused 8 times with maintaining reactivity. Further photochemical reactions using this privileged photocatalyst under visible light are being pursued in our laboratory.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Author contributions

The manuscript was written through the contributions of all authors. All authors have approved the final version of the manuscript.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.mcat.2021.111810.

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